**Application No.:** 10/825,881

Office Action Dated: January 9, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application. Listing of Claims:

## 1. (Currently amended) A compound of formula I:

$$R_6$$
 $X$ 
 $R_4$ 
 $Y$ 
 $Z$ 
 $R_1$ 
 $R_2$ 
 $R_5$ 
 $R_3$ 
 $I$ 

or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof;

wherein independently,

 $R_1$  and  $R_2$  are: H, lower alkyl, cyclic alkyl, or benzyl;

Y is  $-[CR_8R_9]_{[[n]]}^-$ , where  $R_8$  is H, and  $R_9$  is aryl optionally substituted with 1-3 substituents selected from the group consisting of lower alkyl, halo, hydroxy, and alkoxy; or benzyl wherein the said phenyl portion thereof is optionally substituted with 1-3 substituents selected from the group consisting of lower alkyl, halo, hydroxy, and alkoxy, and n is 1.;

Z is:  $-[C(R)_2]_n$ -, CHOR, O, S, NR, CONH, or NHCO;

 $R_3$ ,  $R_4$ ,  $R_5$ , and  $R_7$  are: H, I, Br, Cl, F, CH<sub>3</sub>, CF<sub>3</sub>, CN, SR, OCH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, or CH(CH<sub>3</sub>)<sub>2</sub>;

 $R_6$  is: OR, H, SH, F, CF<sub>3</sub>, lower alkyl, or  $N(R)_2$ ;

X is: O, S, SO, SO<sub>2</sub>, NR,  $C(R)_2$ , –lower alkyl-O-, -O-lower alkyl-, COCH<sub>2</sub>O, or OCH<sub>2</sub>CO; and

R is H, lower alkyl, aryl optionally substituted with 1-3 substituents selected from the group consisting of lower alkyl, halo, hydroxy, and alkoxy; or benzyl wherein the said phenyl portion thereof is optionally substituted with 1-3 substituents selected from the group consisting of lower alkyl, halo, hydroxy, and alkoxy; and

n is 1 to 6; and

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provided that the compound is not thyronamine, 3,5-diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3',5'-tetraiodothyroethanolamine, 3,5,3'-triiodothyroethanolamine, or 3,5-diiodothyroethanolamine.

- 2. (original) The compound of claim 1, wherein  $R_4$  and  $R_5$  are H,  $CH_3$ ,  $CF_3$ , CN,  $OCH_3$ ,  $CH_2CH_3$ , or  $CH(CH_3)_2$ .
  - 3. (Currently amended) The compound of claim 2, wherein  $R_1$  and  $R_2$  are H,  $R_3$  is I,  $R_4$ ,  $R_5$ , and  $R_7$  are H,  $R_6$  is OH, X is O,  $\frac{1}{2}$  and Z is are each CH<sub>2</sub>.
  - 4. (original) The compound of claim 1, wherein R<sub>4</sub> is H, CH<sub>3</sub>, CF<sub>3</sub>, CN, OCH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, or CH(CH<sub>3</sub>)<sub>2</sub>; and R<sub>5</sub> is I, Br, Cl, or F.
  - 5. (Currently amended) The compound of claim 4, wherein  $R_1$  and  $R_2$  are H,  $R_4$  and  $R_7$  are H,  $R_3$  and  $R_5$  is I,  $R_6$  is OH, X is O,  $\frac{1}{2}$  and Z is are each CH<sub>2</sub>.
  - 6. (Currently amended) The compound of claim 4, wherein  $R_1$  and  $R_2$  are H,  $R_4$  is H,  $R_3$ ,  $R_5$ , and  $R_7$  are I,  $R_6$  is OH, X is O,  $\frac{1}{2}$  and Z is are each CH<sub>2</sub>.
  - 7. (original) The compound of claim 1, wherein  $R_1$  is lower alkyl,  $R_6$  is OH or OR, and X is O.
  - 8. (original) The compound of claim 1, wherein  $R_3$  is a halogen,  $R_6$  is H, and X is O.
  - 9. (original) The compound of claim 1, wherein X is alkoxy.
  - 10. (original) The compound of claim 1, wherein  $R_1$  and  $R_2$  are H or lower alkyl,  $R_6$  is H or  $CF_3$ , and X is alkoxy.
  - 11. (Currently amended) The compound of claim 1, wherein  $R_1$  is H or lower alkyl, and Y is  $C(R)_2$ .
  - 12. (Currently amended) The compound of claim 1, wherein  $R_1$  and  $R_2$  are H or lower alkyl,  $R_6$  is H, X is O,  $\frac{Y}{100}$  is alkyl.

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13. (Currently amended) The compound of claim 1, wherein  $\frac{Y}{Y}$  is  $-[C(R)_2]_{n-1}$  where R  $R_0$  is aryl and n is 1 optionally substituted with 1-3 substituents selected from the group consisting of lower alkyl, halo, hydroxy, and alkoxy.

## Claims 14-21 canceled

- 22. (Currently amended) A pharmaceutical composition, comprising at least one pharmaceutically acceptable carrier or excipient and at least one compound of claim 1, elaim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5-diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3',5' tetraiodothyroethanolamine, 3,5,3'-triiodothyroethanolamine, or 3,5-diiodothyroethanolamine to the subject.
- 23. (Withdrawn, Currently amended) A method of exerting a positive inotropic effect on the heart without affecting the heart rate of a mammalian subject comprising the step of administering to said subject an effective amount of the compound of claim 1, claim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5 diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3',5' tetraiodothyroethanolamine, 3,5,3'-triiodothyroethanolamine, or 3,5 diiodothyroethanolamine.
- 24. (Cancelled)
- 25. (Withdrawn, Currently amended) A method of lowering the core body temperature of a mammalian subject comprising the step of administering to said subject an effective amount of the compound of claim 1, claim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5-diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3',5'-tetraiodothyroethanolamine, 3,5,3'-triiodothyroethanolamine, or 3,5-diiodothyroethanolamine.
- 26. (Withdrawn, Currently amended) The method of claim <u>25</u> [[9]], wherein administering the compound of claim 1 induces torpor or hibernation in said subject.
- 27. (Withdrawn, Currently amended) A method of treating a mammalian subject during surgery comprising administering to the subject a therapeutically effective amount of the Page 5 of 12

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compound of claim 1, claim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5-diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3'-5'-tetraiodothyroethanolamine, 3,5,3'-triiodothyroethanolamine, or 3,5-diiodothyroethanolamine, or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof.

- 28. (Withdrawn) The method of claim 27, wherein said method reduces the core body temperature and induces anesthesia in the subject.
- 29. (Withdrawn) The method of claim 27, said method reduces blood loss of the subject.
- 30. (Withdrawn, Currently amended) A method for alleviating a disease state in a mammal believed to be responsive to treatment with a thyronamine agonist comprising the step of administering to the mammal a therapeutic amount of the compound of claim 1, claim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5 diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3',5'-tetraiodothyroethanolamine, 3,5,3'-triiodothyroethanolamine, or 3,5 diiodothyroethanolamine, or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof.
- 31. (Withdrawn, Currently amended) The method of claim 30, wherein the compound said composition is an agonist of a G protein coupled receptor.
- 32. (Withdrawn, Currently amended) The method of claim 31, wherein the compound said composition is an agonist of a trace amine receptor.
- 33. (Withdrawn, Currently amended) The method of claim 30, wherein the disease state is congestive heart failure, cardiac arrhythmia, or stroke.

34-35. (Cancelled)

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36. (Withdrawn, Currently amended) The method of claim 30, wherein the disease state is diabetes, hyperglycemia, hypoglycemia, eardiae arrhythmia, stroke, osteoporosis, or obesity, atherosclerosis, hypertension, hyperthyroidism or hypothyroidism.

- 37. (Withdrawn, Currently amended) A method for alleviating a disease state in a mammal believed to be responsive to treatment with a thyronamine antagonist comprising the step of administering to the mammal a therapeutic amount of the compound of claim 1, claim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5 diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3',5' tetraiodothyroethanolamine, 3,5,3' triiodothyroethanolamine, or 3,5 diiodothyroethanolamine, or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof.
- 38. (Withdrawn, Currently amended) The method of claim 37, wherein the compound said composition is an antagonist of a G protein coupled receptor.
- 39. (Withdrawn, Currently amended) The method of claim 38, wherein the compound said composition is an antagonist of a trace amine receptor.
- 40. (Withdrawn, Currently amended) The method of claim 37, wherein the disease state is congestive heart failure, cardiac arrhythmia, or stroke.
- 41-42. (Cancelled)
- 43. (Withdrawn, Currently amended) The method of claim 37, wherein the disease state is diabetes, hyperglycemia, hypoglycemia, eardiac arrhythmia, stroke, osteoporosis, or obesity, atherosclerosis, hypertension, hyperthyroidism or hypothyroidism.
- 44. (Withdrawn, Currently amended) A method of treating a mammalian subject during open heart surgery believed to be responsive to treatment with a thyronamine antagonist comprising administering a therapeutically effective amount the compound of claim 1, claim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5-diiodothyronamine, 3,5,3'-

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triiodothyronamine, thyroxamine, 3,5,3',5' tetraiodothyroethanolamine, 3,5,3' triiodothyroethanolamine, or 3,5 diiodothyroethanolamine, or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof, to the subject.

- 45. (Withdrawn, Currently amended) A method of treating a mammalian subject during trauma or blood loss believed to be responsive to treatment with a thyronamine antagonist comprising administering a therapeutically effective amount the compound of claim 1, claim 14, claim 16, claim 18, or claim 21, or thyronamine, 3,5-diiodothyronamine, 3,5,3'-triiodothyronamine, thyroxamine, 3,5,3',5' tetraiodothyroethanolamine, 3,5,3'-triiodothyroethanolamine, or 3,5-diiodothyroethanolamine, or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N oxide or isomorphic crystalline form thereof, to the subject.
- 46. (Currently amended) An isotopically labeled compound of claim 1, claim 14, claim 16, claim 18, or claim 21.
- 47. (original) The compound of claim 46 isotopically labeled with <sup>3</sup>H, <sup>2</sup>H, or <sup>125</sup>I.
- 48-58. (Cancelled)
- 59. (Currently amended) The compound of claim 1, wherein  $R_9$  is benzyl wherein the said phenyl portion thereof is substituted with hydroxyl.
- 60. (Previously presented) The compound of claim 59 wherein,  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_5$ , and  $R_7$  are H,  $R_4$  is I,  $R_6$  is hydroxyl, X is O, and Z is  $CH_2$ .